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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/306,420	05/06/1999	STEPHEN A. LOCARNINI	2551-28	3419

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EXAMINER
MOSHER, MARY

ART UNIT	PAPER NUMBER
1648	21

DATE MAILED: 12/17/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/306,420	Locarnini et al
Examiner	**Art Unit**
Mary Mosher	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *10/9/01, 4/26/01* .

2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *32-54* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *46* is/are allowed.

6) ☒ Claim(s) *32-41, 44, 45, and 47-54* is/are rejected.

7) ☒ Claim(s) *42 and 43* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *18*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

Claims 32-34, 37-39, 41, 44, 45, 47-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32, 44, and 50 are confusing, for several reasons. First, it is not clear what scope is intended. Each claim recites a mutant *comprising* a mutation resulting in an amino acid change in the part of the polymerase *consisting essentially of* the B domain. Which statement of scope is intended, comprising or consisting essentially of? Is the claim open to mutations outside of the B domain, or not?

Second, the intended scope of "the B domain" is not clear. In applicant's response, page 12, last sentence, the response states that "The B domain spans approximately 20 amino acids..." However, the specification states on page 6 that "The B domain is considered to comprise amino acids 505 to 529 of HBV DNA polymerase....Reference to the B domain includes reference to the proximal regions which includes up to about 20 amino acids on either side of the domain." So does the B domain include 20 amino acids, 25 amino acids (residues 505-529), or 65 amino acids (residues 485-549)? What are the boundaries of the B domain?

Third, it is even less clear what scope is intended for "consisting essentially of the B domain". While there is a general understanding of the meaning of the legal term "consisting

essentially of" in defining the ingredients in a composition, it is not clear what is meant by "consisting essentially of" a domain in defining the location of mutations in HBV isolates.

For these reasons, the claims do not reasonably apprise one skilled in the art of the scope and content of the subject matter that applicant wishes to claim. This affects the claims dependent from claims 32, 44, and 50.

In claims 33 and 34, it still is not clear if the recited sequence defines the sequence before mutation or after mutation.

Claim 37 and 38 are indefinite because they lack a sequence identifier for the recited sequence. This affects the dependent claims.

Claim 41 lacks antecedent for "said nucleoside analog", since parent claim 40 describes the mutant strictly in terms of structure, not in terms of nucleoside resistance.

Claim 45 is incomplete, as it lacks an interpretation step. This affects the dependent claims.

Would language such as this better describe the invention of claims 32-34?

A. An isolated HBV mutant, comprising a mutation in the gene encoding the DNA polymerase resulting in decreased sensitivity to a nucleoside analog compared to wild-type HBV, wherein said mutation results in at least one amino acid addition, substitution, and/or deletion in the B domain corresponding to amino acid residues 505-529 of wild-type HBV polymerase.

B. An isolated HBV mutant according to claim A, wherein the mutation is located in the region corresponding to SEQ ID NO:25

C. An isolated HBV mutant according to claim A, wherein the mutation is located in the region corresponding to SEQ ID NO:44.

Claim 54 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "new matter" rejection. Applicant is requested to point to support for the claim in the specification as filed, as no description of a drug screening assay using mutated non-HBV Hepadnaviruses is apparent to the examiner.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 32-41, 50, and 51 are rejected under 35 U.S.C. 102(a) as being anticipated by Ling et al. Ling et al is still available as prior art, being published in September 1996. Ling teaches lamuvidine-resistant HBVs which comprise Phe512Leu or Leu526Met mutations in the B domain of the polymerase. Ling does not state that these mutations are responsible for the resistance; however, the claims, as written, do not exclude other mutations. Ling further does not state that these mutations affect resistance to other nucleoside analogs such as famciclovir; however, the drug-resistance phenotype is an inherent characteristic of the mutant virus, even if the reference

does not disclose that characteristic. Therefore the reference anticipates the mutant virus, as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 45, 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ling et al. Claim 45 is drawn to a method for detecting drug-resistance mutations, and excludes the specific combinations of M550V + L526M (Ling's patient 1) and M550I + F512L or V553I (Ling's patient 2). However, since multiple mutations are not unusual in persistent HBV, one of ordinary skill in the art would have been motivated to screen potentially resistant viruses for combinations of mutations in the M550 residue of YMDD with secondary mutations in residues

512, 526, and/or 553. Therefore one of ordinary skill would have been motivated to include screening for the combination of M550V with F512L, for example, even if the first patient found with F512L combined it with M550I. In other words, the teachings of Ling et al are not limited to the specific combinations disclosed in the two patients, but also suggest other possible combinations of mutations at the same sites. This affects dependent claims 47-49.

Allowable Subject Matter

Claim 46 is allowed.

Claims 42 and 43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter:

Claims 42-43 are free of the prior art, because Ling et al does not teach mutation in polymerase residue 499, or mutations that cause the specific surface antigen mutations, as recited in these claims. Claim 46 is free of the art, because Ling et al teaches mutations involved in lamividine resistance, and does not teach or suggest that the specific mutations indicate pencyclovir or famciclovir resistance

Claim 44 is also free of the art, because Ling et al points to mutations in YMDD (in the C domain), not the mutations in the B domain, as indicating reduced drug sensitivity.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 14, 2001

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600